Remarks

Amendments to the Claims

Claims 27, 56, 62, 63 are amended to recite "an mRNA comprising nucleotides 312-1784 of SEQ ID NO:2 and encoding human MDM2" in place of "a coding sequence for human MDM2." New claim 64 also contains this recitation. Nucleotides 312-1784 of SEQ ID NO:2 is the coding sequence for human MDM2 (see the sequence listing filed with the application). New claims 64-67 recite "at least 34 contiguous nucleotides," which is supported by the alignment in FIG. 1A (nucleotides 356-389).

The amendments do not add new matter.

Sequence Listing

The paper copy of the sequence listing filed with this application contains five (5) sequences. The supplemental content in PAIR contains two text versions of the sequence listing: one has four (4) sequences, the other has five (5) sequences. The sequence listing with five (5) sequences corresponds to the paper copy of the sequence listing as filed. "SEQ ID NO:2" recited in the pending claims refers to SEQ ID NO:2 of the sequence listing as filed.

Rejection of Claim 28 Under 35 U.S.C. § 112 ¶ 2

Claim 28 stands rejected under 35 U.S.C. § 112 ¶ 2 as indefinite. Claim 28 was canceled to advance prosecution, which renders the rejection moot.

Rejection of Claims 27, 28, 56, 62, and 63 Under 35 U.S.C. § 112 ¶ 1

Claims 27, 28, 56, 62, and 63 stand rejected under 35 U.S.C. § 112 ¶ 1 as insufficiently described. Applicants respectfully traverse the rejection.

Each of the pending claims recites a genus of antisense oligonucleotides. The Final Office Action contends the genus is not sufficiently described because there is no "specific biochemical or molecular structure that could be envisioned by one skilled in the art." Final Office Action at page 2, last paragraph. This is simply not correct. In fact, the analysis provided in Example 15 ("Antisense") of the PTO's Written Description Training Guidelines can be applied directly to the pending claims. Example 15 analyzed whether the following hypothetical claim met the written description requirement:

> An antisense oligonucleotide complementary to a messenger RNA having SEQ ID NO:2 and encoding human growth hormone, wherein said oligonucleotide inhibits the production of human growth hormone.

Similarly, the pending claims recite "antisense oligonucleotides which are complementary to an mRNA having nucleotides 312-1784 of SEQ ID NO:2 and encoding human MDM2 and which inhibit expression of human MDM2 protein." The pending claims meet the written description requirement for the same reasons the PTO determined that the hypothetical claim in Example 15 meets the requirement.

Whether a specification meets the written description requirement is a question of fact. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991). Compare the facts in this case with those in Example 15 of the Written Description Training Guidelines:

Example 15	this application
claim: "An antisense oligonucleotide complementary to a messenger RNA having SEQ ID NO:2 and encoding human growth hormone, wherein said oligonucleotide inhibits the production of human growth hormone."	claim 27. An *in vitro* method of treating a neoplastic cell, comprising: administering to the cell a therapeutically effective amount of antisense oligonucleotides which are complementary to: an mRNA comprising nucleotides 312-1784 of SEQ ID NO:2 and encoding human MDM2, and which inhibit expression of human MDM2 protein.
"specification discloses a messenger RNA sequence, SEQ ID NO:1, which encodes full-length human growth hormone"	specification discloses a nucleotide sequence that encodes full-length human MDM2 (SEQ ID NO:2)
"specification states that the invention includes antisense molecules that inhibit the production of human growth hormone"	specification discloses that the invention includes antisense oligonucleotides that prevent transcription or translation of human MDM2; *i.e.*, they inhibit expression of MDM2 protein (see page 10, lines 22-26)
"The general knowledge in the art is that any full-length complement of a target mRNA inhibits the function of the mRNA and is therefore an antisense oligonucleotide. Thus, one of skill in the art would view applicant's disclosure of a coding sequence, with the statement that the invention includes antisense oligonucleotides, as an implicit disclosure that the full-length complement of SEQ ID NO:1 is an antisense oligonucleotide."	by disclosing SEQ ID NO:2, the present specification inherently describes a single species of oligonucleotide with a complete structure, *i.e.*, the full-length complement of SEQ ID NO:2
"In addition to the full-length complement, the genus includes fragments of the complement that retain antisense activity."	genus of antisense oligonucleotides recited in pending claims includes fragments that retain antisense activity
"It is generally accepted in the art that oligonucleotides complementary to a messenger RNA, including fragments of the full-length complement, have antisense activity when they match accessible regions on the target mRNA."	applies with equal force at April 4, 1992 priority date of this application[1]
"Generally, the closer the complementary fragment is to full length, the greater the likelihood it will have antisense activity."	applies with equal force at April 4, 1992 priority date of this application[2]

[1] See Shuttleworth & Colman, *EMBO Journal 7*, 427-34, 1988 (cited in IDS accompanying this paper).

[2] See Stein & Cohen, *Cancer Res. 48*, 2659-68, May 15, 1988 (cited in IDS accompanying this paper).

"[O]ligonucleotides that retain complementarity to the Shine-Delgarno sequence usually have antisense activity."	applies with equal force at April 4, 1992 priority date of this application[3]
"The procedures for making oligonucleotide fragments of the SEQ ID NO:1 complement are conventional, e.g., any specified fragment can be ordered from a commercial synthesizing service."	applies with equal force at April 4, 1992 priority date of this application[4]
"The procedures for screening for antisense activity are also conventional, and the specification describes the assay needed to do gene walking."	procedures for screening for antisense activity, including "gene walking," were known in the art at this application's April 4, 1992 priority date[5]
"[T]he sequence provided in the specification defines and limits the structure of any effective antisense molecules."	SEQ ID NO:2 defines and limits the structure of any effective antisense molecules: each such effective molecule must be complementary to an mRNA having nucleotides 312-1784 of SEQ ID NO:2

Example 15 concludes that one skilled in the art would conclude that applicants were in possession of the invention in light of: (1) the specification's disclosure of the full-length sequence, which defines and limits the structure of any effective antisense molecules such that one skilled in the art would be able immediately to envisage members of the genus embraced by the claim, (2) the functional characteristics of the claimed invention as well as a routine art-recognized method of screening for antisense molecules which provide further distinguishing characteristics of the recited antisense molecules, and (3) the general level of knowledge and skill in the art. The identical facts apply here. Thus, as the PTO concludes in Example 15, the specification adequately describes the recited genus of antisense oligonucleotides.

[3] See Hirashima *et al.*, *J. Biochem. 106*, 163-66 (1989) (cited in IDS accompanying this paper).

[4] See Bjergård & Dahl, *Nucl. Acids Res. 19*, 5843-50, 1991 (cited in IDS accompanying this paper).

[5] See Parker *et al.*, *Nucl. Acids Res. 19*, 3055-60, 1991 (cited in IDS accompanying this paper).

This argument applies with equal force to new claims 64-67. Please withdraw the rejection.

Respectfully submitted,

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